<table>
<thead>
<tr>
<th>項目</th>
<th>内容</th>
</tr>
</thead>
<tbody>
<tr>
<td>項目</td>
<td>放熱反応に於ける視床下部温度の役割</td>
</tr>
<tr>
<td>名称</td>
<td>井元 孝章</td>
</tr>
<tr>
<td>項目</td>
<td>熱帯医学 トロピカルメディシン  humane tropical medicine</td>
</tr>
<tr>
<td>項目</td>
<td>熱帯医学 トロピカルメディシン  humane tropical medicine</td>
</tr>
<tr>
<td>項目</td>
<td>熱帯医学 トロピカルメディシン  humane tropical medicine</td>
</tr>
<tr>
<td>項目</td>
<td>熱帯医学 トロピカルメディシン  humane tropical medicine</td>
</tr>
<tr>
<td>項目</td>
<td>熱帯医学 トロピカルメディシン  humane tropical medicine</td>
</tr>
</tbody>
</table>
The Influence of Hypothalamic Temperature on Thermal Panting in the Rabbit*

Takaakira INOMOTO

Department of Epidemiology, Institute for Tropical Medicine, Nagasaki University

Abstract: The influence of hypothalamic temperature (Thy) on respiratory evaporative heat loss (REHL) was studied on conscious rabbits equipped with a hypothalamic thermode. At an ambient temperature of 39°C, the animal’s esophageal temperature (Tc) was maintained at a hyperthermic level of 40 or 41°C by controlled heat extraction with an intestinal thermode. At each constant Tc, 2-3 min cooling of the hypothalamus was performed with a thermode perfusion temperature (Tperf) of 35 or 30°C, and respiratory rate (RR) was recorded as the parameter of REHL. Under the experimental conditions, it was presumed that Tc represented all extrahypothalamic temperatures (Tex), because skin temperatures barely differed from Tc. The experimental results, when RR was described as a function of Tex at each Tperf, could clearly demonstrate that a slope indicating the sensitivity for heat dissipation response to a unit change of Tex was smaller at a lowered Thy (Tperf=30°C) than that determined at 35°C Tperf. This indicates a reduced sensitivity for heat dissipation activity in response to changes of Tex with decreasing Thy as predicted from the idea that intrahypothalamic signal transmission is temperature dependent.

Key words: Thermoregulation, hypothalamic temperature, extrahypothalamic temperature, thermosensory function, panting.

INTRODUCTION

In mammals, cooling the preoptic anterior hypothalamus elicits cutaneous vasoconstriction and shivering. Several conventional models describing the known thermoregulatory responses by interaction between hypothalamic and extrahypothalamic temperatures have exclusively been based on the assumption that in the hypothalamus, signal which originates from hypothalamic thermoreceptive neurons is the only element responsible for providing the apparent thermosensory function. However, the hypothalamic thermosensory function can also be explained by assuming the existence of a temperature...
dependent intrahypothalamic signal transmission (Hammel, 1968). Recently, based on
the latter hypothesis, a mathematical neuronal model of thermoregulation has been pro-
posed by Simon (1981). The model for mammals presumes a greater $Q_{10}$ of cold than
warm pathway conveying afferent signals from extravertical tissues as well as from
the hypothalamus itself.

Fig. 1 presents the results of the previous study which was designed to experi-
mentally prove the above proposition in a mammalian species, the rabbit
(Inomoto et al., 1982). According to
Simon's model, lowering hypothalamic
temperature would suppress more cold
signal than warm signal transmission,
thereby exhibiting a reduced sensitivity
for any thermoregulatory effector activity
responding to a given change of extra-
hypothalamic temperature. In the dia-
gram, one can clearly see that at a low-
ered hypothalamic perfusion temperature
($T_{perf}=30^\circ C$), the slope, indicating the
sensitivity with which cold defense (me-
tabolic heat production; $M$) drives in response to changes of extravertical tempe-
ratuere ($T_c$), is smaller as compared to that at a normal hypothalamic temperature
($T_{perf}=39^\circ C$). On the other hand, the threshold $T_c$ for the response is increased
because of the existence of primary hypothalamic thermoreceptors.

The purpose of the present study was to test whether the prediction is also true
for heat dissipation by investigating the control of panting by interaction of hypothalamic
and extravertical temperatures on conscious rabbits equipped with a hypothalamic
perfusion thermode.

**Fig. 1. Relation between metabolic heat produc-
tion ($M$), core temperature ($T_c$) and
hypothalamic temperature ($T_{perf}$) in
conscious rabbits at an air temperature
of 10 °C. From Inomoto et al. (1982).**

**MATERIALS AND METHODS**

The experiments were carried out on four rabbits (*Viennese Grey*) with an average
body weight of 3.6 Kg in a climatic chamber at a hot (39°C) air temperature. Between
the experiments the animals were housed in individual cages at thermoneutrality (22°C).
Each animal was provided chronically with a hypothalamic thermode consisting of four
blind ending stainless-steel tubes. The implantation procedure and the verification of
the thermode's position in the preoptic anterior hypothalamic (PO/AH) region were de-
scribed elsewhere (Inomoto et al., 1982). As rabbits can not maintain thermal balance
despite the onset of panting under the experimental condition of 39°C ambient temperature (Stitt, 1976), an intestinal cooling thermode was used to extract excess heat from the animal. The thermode consisted of three U-shaped polyethylene tubes (Portex PP 200) and was inserted 20 cm deep into the colon. By altering temperature and flow rate of water perfusing the thermode, the animal's core temperature could be maintained at a certain hyperthermic level.

Fig. 2 illustrates the experimental setup. Temperatures of air (Ta), hypothalamic thermode perfusion (Tperf), ear and back skin, and body core (Tc) were measured with iron-constantan thermocouples. Esophageal temperature was measured as a representative of Tc with a thermocouple introduced via the nasal cavity. Respiratory rate (RR) was picked up by recording impedance changes in an electrolyte-filled distensible rubber tube placed around the animal's thorax. The experiments were carried out on the animals restrained in a conventional rabbit box. The animals exposed to the severe heat stress were allowed to stay for 1–2 hr so that their Tc could be raised while hypothalamic temperature (Thy) was clamped at an approximately normal level by perfusing continuously the hypothalamic thermode with water of 39°C. At a given hyperthermic level of Tc thus attained, intestinal cooling was started in order to maintain the animal's Tc either at about 40 or 41°C. When the animals were in stable conditions, stepwise displacements of Thy were performed by lowering Tperf, from 39°C to 34 or 39°C, with three heat exchanger-thermostat systems and the RR was continuously recorded.

RESULTS

The time course of a single experiment is shown in Fig. 3. After the animal had been exposed to an ambient temperature of 39°C with a Tperf of 39°C in a climatic chamber, it took about one hour to reach a hyperthermic level of 40°C Tc. When the animal came into thermally stable conditions, as indicated by constant panting rate (RR) and core temperature (Tc) of 450 cycles per minute and 40.3°C respectively, hypothalamic cooling with a Tperf of 30°C was performed for two minutes. From provisional experiments a cooling period longer than three minutes had been confirmed to cause Tc elevation due to suppressed respiratory evaporative heat loss, the secondary change in
Tc interfering the primary effect of the stimulation. It is noted in the figure presenting a two-minute-experiment that lowering Thy inhibited thermal panting with no subsequent change in Tc during the cooling period.

Thus, a total of fifty-five alterations of Tperf from 39°C to 34 or 30°C for 2-3 min was made on four conscious rabbits and the RR value was taken from the last minute of the stimulation period as the experimental value. A maximum panting rate of approximately 420 cycles per minute was attained when Tperf was above 34°C at a clamped Tc level of about 41°C, corresponding to that from rabbits subjected to whole body heating (Kosaka et al., 1983). Therefore, the respiratory rate corresponding only to 34 or 30°C Tperf were separately grouped and averaged according to Tc levels, i.e., 40°C and 41°C, and were served to a statistical analysis.

The results of the experiments are summarized in Fig. 4, showing the correlations between RR and Tc at 34 and 30°C Tperf. In the diagram, each slope indicates a gain for heat dissipation response to a given change of Tc at a hypothermic level of Thy. It can be seen that the slope of the upper line (A) determined at a Tperf of 34°C is greater than that of the lower line (B) at a further decreased perfusion temperature of 30°C; 0.71°C rise in Tc induced an increase of RR by 91 on average at a Tperf of 34°C, while on average only 55 increase in RR resulted from 0.84°C change in Tc at a Tperf of 30°C. This
difference is statistically significant ($t$-test, $P < 0.05$). Thus, a reduction of gain for thermoregulatory effector activity responding to $T_{ex}$ changes with decreasing $T_{hy}$ was experimentally confirmed to be also true for heat dissipation as already demonstrated for metabolic heat production in rabbits by Inomoto et al. (1982).

**DISCUSSION**

The control of heat defense was investigated on conscious rabbits exposed to a severe heat stress. $RR$ was chosen as the parameter for respiratory evaporative heat loss ($REHL$) in the present experiments, because $RR$ is the most rapidly responding parameter whose reactions to $T_{hy}$ displacements can be detected before secondary fluctuations in $T_c$ occur. Furthermore, $RR$ can be presumed to be proportional to $REHL$ under thermal panting from the study of Thiele and Albers (1963). At the ambient temperature under study, various body temperatures continued to rise passively until $T_c$ measured in the esophagus could be presumed to represent all $T_{ex}$ including skin temperatures. By using an intestinal cooling thermode it was possible to keep the animal’s $T_c$ in a hyperthermic range (40-41°C), while selective thermal stimulation of the hypothalamus was performed. Thus, the present experimental conditions enabled a study to investigate the regulation of $REHL$ by interaction of $T_{hy}$ and accurately defined $T_{ex}$ in a wide range of hyperthermia.

The present study experimentally proved that the sensitivity with which the autonomic heat defense activity responds to $T_{ex}$ changes decreased with decreasing $T_{hy}$. Any mathematical model of thermoregulation can not explain the present as well as the preceding (Inomoto et al., 1982) results unless the property of the hypothalamic thermostat is incorporated in the model (Simon, 1981; Simon et al., 1983). A new concept concerning the hypothalamic thermosensory function is derived from numerous studies on birds. Although the ability of autonomic heat and cold defense is equal in birds and mammals (Inomoto and Simon, 1981), the two classes differ in their thermosensory function of the hypothalamus. In birds, lowering $T_{hy}$ induces skin vasodilatation and suppression of shivering, contrary to mammals (for review see Simon-Oppermann, 1978). The paradoxical effects of PO/AH cooling has on avian thermoregulation were ascribed to a non-specific temperature dependence of hypothalamic neuronal network and to the non-existence of cold receptors in the hypothalamus. Recently, Lin and Simon (1982) directly demonstrated a higher $Q_{10}$ of cold signal than warm signal pathway in the duck’s hypothalamus. If one accepts that birds and mammals may have inherited the same neural arrangement in the CNS thermoregulatory network from their ancestors, the opposing effects of hypothalamic cooling on avian and mammalian effector activities can be explained by additionally assuming the existence of *primary* thermoreceptors in the mammalian hypothalamus (Simon, 1981). Concerning the primary thermoreceptors, no direct
demonstration has been made yet, however, a body of evidences seems to support indirectly their probable existence (for discussion see Inomoto et al., 1982). Decreased intensities of thermoregulatory activities at a hypothermic level of Thy was also demonstrated in birds (Simon-Oppermann and Simon, 1980). According to the model of Simon (1981), the control of thermoregulatory responses can be described by an additive interaction between hypothalamic and extrahypothalamic temperature signals, both being further modified in their afferent pathways, cold and warm, by local hypothalamic temperature.

ACKNOWLEDGEMENTS

The author would like to thank Professor Eckhart Simon and Doctor James B. Mercer in the Max-Planck-Institute, Bad Nauheim, West Germany and Professor Mitsuo Kosaka in the Department of Epidemiology for their continuous kind support and encouragement for this study. The author’s thanks are extended to the staff in the Department of Epidemiology for their kind help.

REFERENCES


放熱反応に於ける視床下部温度の役割
井元孝章（長崎大学熱帯医学研究所疫学部門）

ウサギを高室温（39℃）に暴露するとパニック発現にかかわらず熱平衡を保てる時温は上昇を続ける。本研究では、腸管内サーモードを用いて余剰の熱を動物から除くことにより一定の高体温（40-41℃）に保ち、視床下部サーモードによる温度刺激を行い、誘起された放射散失反応の指標として呼吸数の変化を測定した。放熱反応と視床下部温度（Thy）及び視床下部外温度（Tex）との関係解析から、Tex 変化に応じて発現するパニック反応の強さは低 Thy 時減弱するとの成績を得た。この実験事実は従来の体温調節モデルにおいては説明不可能であり、近年提唱された視床下部体温調節中樞に於ける温度信号伝達路の非特異的局所温度依存性の概念を実証したものである。

熱帯医学 第25卷 第 2 号, 99-105頁, 1983年 6月